

**Memorandum of Understanding**

between

**DuPont Pharmaceuticals Company**

and

**Public Health Service**

**U.S. Department of Health and Human Services**

This Memorandum Of Understanding (hereinafter " Agreement" ), effective this first day of July 1998, by and between the Public Health Service of the U.S. Department of Health and Human Services as represented by the Office of Technology Transfer, having an address at National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852 (" PHS" ) and DuPont Pharmaceuticals Company, a Delaware general partnership having a principal place of business at Chestnut Run Plaza, Walnut Run, 974 Centre Road, Wilmington, Delaware 19807 (" DuPont" ), a wholly owned subsidiary of E.I. DuPont de Nemours & Co. PHS and DuPont are referred to herein as the " Parties" .

WHEREAS DuPont scientists have developed certain technologies described, embodied by and claimed in U.S. Patent 4,959,317 concerning site-specific recombination of DNA using cre recombinase and lox sites in eukaryotic cells, that have usefulness in basic research conducted or funded by PHS as well as utility for commercial applications; and

WHEREAS PHS has a basic mission on behalf of the U.S. government for the conduct and financial support of health research performed at its own facilities or through funding agreements to other institutions (" Recipient Institutions" ); and

WHEREAS U.S. Patent 4,959,317 and any patents granted on any divisional and continuation applications thereof (" DuPont Patent Rights" ) have been assigned to DuPont; and

WHEREAS the Parties have discussed how DuPont could receive appropriate value from the commercial applications of DuPont Patent Rights without placing undue restrictions or burdens upon health research conducted or funded by PHS.

NOW, THEREFORE, the Parties hereby agree to the following terms and conditions regarding use of DuPont Patents Rights for research conducted by PHS or Recipient Institutions:

(1) DuPont agrees that PHS can use without cost the DuPont Patent Rights for its noncommercial biomedical research purposes, provided however, that such research purposes specifically excludes:

(a) use of cre DNA and/or lox DNA in higher plants or agricultural applications;

(b) use of cre DNA and/or lox DNA in the alteration of mouse embryonic stem cells or other pluripotential mouse cells for the purpose of preparing a library of such mouse embryonic stem cells or other pluripotential mouse cells containing cre DNA and/or lox DNA; and

(c) use of any material containing cre DNA and/or lox DNA which is encompassed by the DuPont Patent Rights ("Material" ) for any commercial purpose or for the direct benefit of any for-profit institution.

The uses set forth in (a), (b) and (c) are outside the scope of this Agreement and shall only be permitted by DuPont under the terms of a separate written agreement between PHS and DuPont or as otherwise permitted to PHS under its authorities as a U.S. government agency.

(2) If in the course of its research program PHS makes a Material that it wishes to transfer to a non-profit institution, PHS agrees that it may do so only under a Material Transfer Agreement incorporating at least the following conditions:

(a) The non-profit institution may use the Material, and any progeny or derivatives containing cre DNA and/or lox DNA derived directly or indirectly therefrom, for its internal noncommercial research purposes only, provided however, that such research purposes specifically excludes (i) any activity associated with higher plants or agricultural applications and (ii) the alteration of mouse embryonic stem cells or other pluripotential mouse cells for the purpose of preparing a library of such mouse embryonic stem cells or other pluripotential mouse cells containing cre DNA and/or lox DNA. The Material, and any progeny or derivatives containing cre DNA and/or lox DNA derived directly or

indirectly therefrom, will not be used for any commercial purpose or for the direct benefit of any for-profit institution (except as may be permitted under a written agreement between the non-profit institution and DuPont).

(b) The Material, and any progeny or derivatives containing cre DNA and/or lox DNA derived directly or indirectly therefrom, may not be transferred by the non-profit institution to any third parties (except as may be permitted under a written agreement between the non-profit institution and DuPont).

(c) The non-profit institution is notified by PHS of the existence of DuPont Patent Rights and that the restrictions set forth under (a) and (b) above shall exist only during the term of the DuPont Patent Rights.

(d) With respect to further license rights under U.S. patent number 4,959,317, the non-profit institution should contact:

Vice President, Product Planning & Acquisition  
DuPont Pharmaceuticals Company  
974 Centre Road, Chestnut Run Plaza, WR722  
Wilmington, Delaware 19807-2802  
(fax number: 302-992-3040)

(3) Notwithstanding (1)(c) above, if in the course of its research program PHS makes a Material that it wishes to transfer to a for-profit institution, PHS agrees that it may do so only under a License or Material Transfer Agreement incorporating at least the following conditions:

(a) The for-profit institution is notified by PHS of the existence of DuPont Patent Rights.

(b) The for-profit institution is notified by PHS that upon its application for a License or Material Transfer Agreement, PHS will be providing notice to DuPont of the identity of both the for-profit institution and the Material to be transferred.

(c) The for-profit institution is notified by PHS that use of the Material, and any progeny or derivatives containing cre DNA and/or lox DNA derived directly or indirectly therefrom, requires a license from DuPont and that a fee (in addition to any fee or royalty payable to PHS) will be

payable to DuPont by the for-profit institution in consideration of transfer of the Material to the for-profit institution (except as may be otherwise permitted under a written agreement between the for-profit institution and DuPont).

(d) No license is granted either expressly or by implication to the for-profit institution by PHS to DuPont Patent Rights.

(e) With respect to license rights under U.S. patent number 4,959,317, the for-profit institution should contact:

Vice President, Product Planning & Acquisition  
DuPont Pharmaceuticals Company  
974 Centre Road, Chestnut Run Plaza, WR722  
Wilmington, Delaware 19807-2802  
(fax number: 302-992-3040)

PHS agrees to provide DuPont prompt notification of the identity of the for-profit institution and the Material to be transferred in accordance with (b) above.

(4) Upon DuPont's written request, PHS agrees to provide without cost reasonable quantities of any Material that it makes in the course of its research program to DuPont for research purposes.

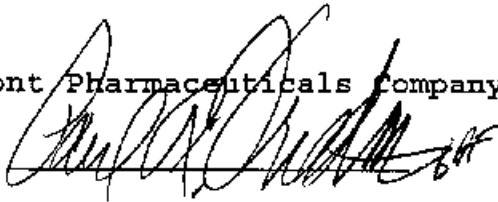
(5) DuPont agrees that it shall make DuPont Patent Rights available for use by Recipient Institutions in accordance with the terms and conditions outlined above. DuPont agrees that it will also notify any non-profit Recipient Institutions currently licensed under DuPont Patent Rights that the non-profit Recipient Institution may amend its license in accordance with the terms and conditions outlined above.

(6) This Agreement and the obligations hereunder shall be in effect only during the term of the DuPont Patent Rights.

IN WITNESS WHEREOF, the Parties agree to the foregoing and have caused this Agreement to be executed by their duly authorized representatives.

DuPont Pharmaceuticals Company

By:



Name: Paul A. Friedman

Public Health Service

By:

Maria Freire 8-10-98

Name: Maria Freire

Title: President, DuPont Pharmaceuticals  
Research Labs

Title: Director, Office of Technology  
Transfer, National Institutes of  
Health